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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/277,401	JAYE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,22,44,57-59,63-65 and 98-103* is/are pending in the application.

4a) Of the above claim(s) *15,16,22,44,57,58,63-65 and 98-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59 and 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: to Applicant - copies

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on June 18, 2004), Applicants filed a response and amendment received on October 21, 2004. Said amendment, amended Claim 59 and cancelled Claims 104-105. Thus, Claims 15, 16, 22, 44, 57-59, 63-65, and 98-103 are pending in the instant Office action.

Election

2. Claims 15, 16, 22, 44, 57-59, 63-65, and 98-103 are pending. Claims 15, 16, 22, 44, 57, 58, 63-65, and 98-102 remain withdrawn from further consideration as non-elected inventions. Claims 59 and 103 will be examined herein.

This application contains claims 15, 16, 22, 44, 57, 58, 63-65 drawn to an invention nonelected with traverse (see response received February 2, 2004. No claims are subject to rejoinder since the elected claims are method claims. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 C.F.R. § 1.144) See M.P.E.P. § 821.01.

Priority

3. As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application Nos. 60/032,254 and 60/032,783 filed on December 6, 1996 and U.S. non-Provisional Application No. 08/985,492 filed on December 5, 1997.

Drawings

4. The drawings, 31 sheets comprising 28 figures, were received on October 21, 2004. These drawings have been entered and accepted by the Draftsman.

Compliance with the Sequence Rules

5. By virtue of Applicant's amendment to the specification, specifically the description of Figure 6, the instant application now fully complies with the sequence rules.

Withdrawn - Objections to the Specification

6. Previous objection to the specification for lacking updated continuity data in the first paragraph is withdrawn by virtue of Applicant's amendment.

7. Previous objection to the specification for being confusing with respect to the sequence listing for the omission of SEQ ID NOs:5 and 9 in the text of the specification is withdrawn by virtue of Applicant's amendment.

Maintained - Objections to the Specification

8. Previous objection to the specification for being confusing about the origin of the LIPG sequences and the SEQ ID NOs is maintained in part with respect to only SEQ ID NOs:5 and 6. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that SEQ ID NOs:5 and 6 are clearly described on page 83 of the specification - this portion is quoted as follows:

> "The overall similarities between this protein [only LLGXL is described up to this point] and the other known members of the triacylglycerol lipase family is illustrated in Figure 6 and Table 1. In the alignment shown in Figure 6, LIPG is the polypeptide (SEQ ID NO: 6) encoded by the cDNA (SEQ ID NO: 5) described in Example 1, and hereafter referred to as LLGN."

The Examiner disagrees that this minimal identification clearly identifies SEQ ID NO:5.

To illustrate the confusion, the Examiner will summarize the examples as found in the specification beginning on page 74 that describe how the SEQ ID NOs have been obtained by the inventors. Example 1 teaches using RT-PCR (differential display) to obtain the cDNA in Figure 2 (SEQ ID NOs:1 and 2); SEQ ID NO:1 is a short fragment of the full-length LIPG open reading frame (ORF). Example 1 further uses 5' RACE extension to obtain a larger portion of the LIPG ORF wherein the cDNA is shown in Figure 3 (SEQ ID NOs:3 and 4); this sequence is still not the complete ORF of LIPG. Example 2 then sets forth the cloning of the complete LIPG ORF (not the cloning of the gene, *per se*, because cDNA, not genomic DNA, is being screened) using the RACE product (SEQ ID NO:3) as a probe. The ORF obtained is described on page 82 as being shown in Figure 4 (SEQ ID NOs:7 and 8), wherein the encoded polypeptide is 500 amino acids long and is called LLGXL.

At this point (see page 83 as quoted above), SEQ ID NOs:5 and 6 are introduced without any indication of how they were obtained. All further examples use the LLGXL sequence, either nucleic acid or protein. Thus, the nature of SEQ ID NO:5 is unclear. Do the inventors consider it an LIPG (i.e. full-length)? Our only indication is found on page 96:

> "The role of the mRNA identified through differential display which encodes a shorter, 40 kD species is not known. There has, however, been a report of an alternately-spliced form of hepatic lipase which apparently is expressed in a tissue-specific manner and would create a truncated protein."

However, this description does not specifically describe the shorter species as SEQ ID NO:6 or LLGN. Thus, the specification is wholly unclear as to the nature of the LLGN LIPG. Clarification is required.

9. Previous objection to the Abstract for not completely describing the disclosed subject matter is maintained and amended. Applicant argues that the amendment has obviated the rejection; the Examiner disagrees. The Abstract, as amended in October 21, 2004, is inadequate because it merely describes the pending claims and not the disclosure as a whole required by M.P.E.P. § 608.01(b). Moreover, it is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of endothelial lipase and the source species, human, for completeness. Correction is required.

10. Previous objection to the amendment filed November 14, 2002 under 35 U.S.C. § 132 because it introduces new matter into the disclosure is maintained. Applicant's arguments have been fully considered but are not deemed persuasive. Applicant argues that support for the five paragraphs inserted at page 25,between lines 7 and 8 can be found on pages 25-27, 29, 30, and 35-36. The Examiner has reprinted Applicant's amendment (named G4) and underlined what cannot be located in these pages, also attached for Applicant's convenience. Page and line number for the amendment is required to show support.

11. Previous objection to the specification for not completely describing the figures 2 and 3 is maintained. Applicant's arguments have been fully considered but are not deemed persuasive. Applicant argues that amendments to the drawings have obviated the rejection; the Examiner disagrees and has identified further inconsistencies.

a) In Figure 2 (see attached copy), the "TTC" circled is described in the sequence listing as the start for the encoded polypeptide, SEQ ID NO:2 - this is not depicted appropriately in the figure. Several amino acid sequences (7-mer at the amino terminus and an 8-mer, a

9-mer, and a 42-mer at the carboxy terminus) are not described by SEQ ID NO since these sequences are not in SEQ ID NO:2. Lastly, the "coding region" defined IS NOT SEQ ID NO:2 since the Gly-Met-Pro at positions 39-41 is missing (see also attached sequence listing). Correction of all these points is required.

b) In Figure 3A-3C (see attached copy), the "ATG" circled is described in the sequence listing as the start for the encoded polypeptide, SEQ ID NO:4 - this is not depicted appropriately in the figure. Two amino acid sequences (99-mer at the amino terminus and a 4-mer at the carboxy terminus) are not described by SEQ ID NO since these sequences are not in SEQ ID NO:4. Lastly, the "coding region" defined IS NOT SEQ ID NO:4 since several omissions of 3-mers are noted (see also attached sequence listing). Correction of all these points is required.

Correction on these points is required.

Withdrawn - Claim Rejections 35 U.S.C. § 112, second paragraph

12. Previous rejection of Claims 59 and 103-105 under 35 U.S.C. § 112, second paragraph, as being indefinite for the relative term "low" is withdrawn by virtue of Applicant's amendment and/or cancellation of said claims.

13. Previous rejection of Claims 105 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicant's cancellation of said claim.

14. Previous rejection of Claims 59 and 103-105 under 35 U.S.C. 112, first paragraph, written description, is withdrawn by virtue of Applicant's amendment of said claim limiting to human LIPG.

15. Previous rejection of Claims 59 and 103-105 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods of identifying human LIPG levels in a human sample, does not reasonably provide enablement for methods of

identifying the genus of LIPG levels in the genus of "patients" is withdrawn by virtue of Applicant's amendment of said claim limiting to human LIPG.

16. Previous rejection of Claims 59 and 103-105 under 35 U.S.C. § 112, first paragraph, enablement, is withdrawn by virtue of Applicant's amendment altering the claim to not require a link between HDL and apolipoprotein AI levels and LIPG.

Maintained - Claim Rejections 35 U.S.C. § 112, second paragraph

17. Previous rejection of Claims 59 and 103 under 35 U.S.C. § 112, second paragraph, as being indefinite for the nature of the human LIPG polypeptide (i.e., its structure) is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the description of LIPG is clearly set forth on page 30 as a lipase enzyme encoded by the LIPG gene. This argument is not persuasive because the nature of the LIPG gene is unclear. See also objection to the specification above for lacking clarity with respect to SEQ ID NOs:5 and 6. Is the LIPG gene SEQ ID NO:7? If so, the Examiner suggests inserting SEQ ID NO:8 into the claim to clearly set forth what the LIPG polypeptide is.

The description on page 30 continues to describe the LIPG polypeptide as follows:

> "The LIPG polypeptide or protein of the invention includes any analogue, fragment, derivative, or mutant which is derived from an LIPG polypeptide and which retains at least one biological property of the LIPG polypeptide."

Nowhere are these biological properties defined. Thus, the definition of LIPG polypeptide is clearly broad and encompasses virtually any lipase, any fragment of SEQ ID NO:8 that induces

antibodies, and polypeptide about 68 kD, and polypeptide having the same expression pattern, etc. as these are all biological properties of SEQ ID NO:8.

Applicant also argues the LLGN and LLGXL are both described on pages 25-26 as being encoded by the LIPG gene; the Examiner can find no such reference.

For all these reasons, the metes and bounds of the LIPG polypeptide are unclear. Is it just SEQ ID NOs: 6 and 8, as seemingly argued by Applicant? Is it any mutant, fragment, derivative, etc. as described on page 30? Clarification is required.

NEW ISSUES

Objections to the Specification

18. The amendment to the drawings filed October 21, 2004 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

a) Newly filed Figures 24-28B. The originally filed specification contained 23 sheets of drawings with a new figure on each sheet (hence Figures 1-23) (see attached copy of Applicant's transmittal document, page 2, filed March 26, 1999). Thus, Figures 24-28B are not supported in the specification as originally filed.
b) The description of SEQ ID NO:5 as "an mRNA product formed from transcription of the human LIPG gene". The only place SEQ ID NOs:5 and 6 are mentioned by name is on page 83, lines 1-4; their origin is not described here.

Applicant is required to cancel the new matter in the reply to this Office Action.

19. The specification is objected to for a typographical error. In the amendment filed October 21, 2004 to include the description of the sequences, in the description of SEQ ID NO:1, the term "PT-PCR" should be ---RT-PCR--- as found in the specification on page 20. Correction is required.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 59 and 103 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ikeda *et al.* (J of Lipid Research (1990) 31:1911-1924). The instant claims are drawn to methods of measuring LIPG in blood using an immunoassay. The instant rejection is set forth considering the broadest reasonable interpretation of the term LIPG polypeptide, as noted above, includes mutants, derivatives, etc. having a biological property of SEQ ID NO:8.

Ikeda *et al.* teach measuring lipoprotein lipase (LPL) in human blood with an immunoassay (see Abstract and page 1912). Human LPL can be considered a human LIPG as interpreted from the specification on page 30 wherein LPL can be derived from SEQ ID NO:8 and has lipase biological activity like LIPG.

The instant rejection had not been previously applied because no correlation with low HDL cholesterol and/or apolipoprotein AI levels is taught by the prior art. Thus, the instant rejection is necessitated by Applicant's amendment.

Conclusion

21. Claims 59 and 103 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Primary Examiner
Art Unit 1652

January 6, 2005